REMARKS

Claims 1 - 31 are pending in the application. Claims 1 – 19 and 30 - 31 have been cancelled. Claims 20 and 29 have been amended.

Any cancellation of the claims should in no way be construed as acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Applicants note that the Examiner has rejoined claims 25 – 27 and claim 19 with elected claims 20 – 24 and 28 (claims set forth in Group I). However, the Examiner then indicates that claims 1 – 19 and 29 – 31 are withdrawn from consideration. Applicants point out that in the Office Action Summary the Examiner has indicated that claims 20 – 29 have been rejected. It is unclear which claims the Examiner has rejoined and which she has rejected.

For the purposes of this response, claims 1 – 31 are pending, claims 1 – 19, 30 and 31 are withdrawn.

The Examiner has indicated that Applicant is required under 37 CFR 1.105 to submit the name of the cDNA microarray that comprises 9,984 human genes provided by Advanced technology as disclosed on page 22 last paragraph" of the disclosure. (form PTO-90C). The Examiner has also asked that Applicant provide information on when this microarray was made available to the public.

In response to this requirement under 37 CFR 1.105, Applicants submit that the cDNA microarray is an internal National Cancer Institute (NCI) microarray that is currently publicly available on the world wide web at ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GPL1262. This human cDNA probe set is based on 9128 PCR products from Incyte's human UniGEM 2.0 library.

35 U.S.C. §112, second paragraph

Claim 29 was rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. (Office Action, p.6). The Examiner argues that "claim 29 recites the limitation 'the method of claim 28' in line 1 (and) there is insufficient antecedent basis for this limitation in the claim because claim 28 is drawn to a product, a microarray, not a method." Applicants respectfully disagree.

Claim 29 has been amended to recite proper antecedent basis. Accordingly, Applicants request that the rejection be withdrawn.

35 U.S.C. §102

Claims 20 and 21 stand rejected under 35 U.S.C. §102(b) over Pederson et al. (British Journal of Cancer, 2001. Vol. 85, No. 8, 1211 – 1218). (Office Action, p.6). Applicants respectfully traverse the rejection.

Claim 20 recites a microarray of genes, or polynucleotide fragments or RNA transcripts thereof for distinguishing a neuroendocrine tumor cell, said microarray comprising a solid support having greater than 10 genes, or polynucleotide fragments or RNA transcripts thereof, distinguishably arrayed in spaced apart regions, wherein said microarray comprises a sufficient number of genes, or polynucleotide fragments or RNA transcripts thereof, that are differentially expressed in a small cell lung cancer (SCLC) cell, a large cell neuroendocrine carcinoma (LCNEC) neuroendocrine tumor cell, a typical carcinoid (TC) neuroendocrine tumor cell, or an atypical carcinoid (AC) neuroendocrine tumor cell, relative to a normal cell or a cell belonging to a different neuroendocrine tumor cell type, to permit said microarray to distinguish a neuroendocrine tumor cell, and wherein said genes or polynucleotide fragments or RNA transcripts thereof includes GGH, or a polynucleotide fragment or RNA transcript thereof.

To anticipate a claim, each and every element of the claim must be found in a single reference. This is discussed in the Manual of Patent Examining Procedure § 2131:

> A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the . . . claim." Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an ipsissimis verbis test, i.e., identity of terminology is not required. In re Bond, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

The Pedersen reference does not teach or suggest all the limitations of the instant claims. In particular, the Pedersen reference does not teach or suggest a microarray of genes, or polynucleotide fragments or RNA transcripts for distinguishing a neuroendocrine tumor cell, as instantly claimed, and where the genes or polynucleotide fragments or RNA transcripts include GGH, or a polynucleotide fragment or RNA transcript thereof..

The Examiner argues that "(t)he GeneChip Hu6800 set, comprising 6800 genes, developed by Affymetrix, comprises genes that are differentially expressed in SCLS cell line GLC-EGFRVIII." The Examiner points out Table 1 that begins on page 1213, and provides a list of genes whose expression is changed more than 2-fold between EGFRvIII- and control cells. None of the genes listed in Table 1 are GGH, as recited in the present claims.

Accordingly, the Pedersen reference does not teach or suggest all the limitations of the instant claims. Applicants respectfully request that the rejection be withdrawn.

Claims 20 – 24 and 27 stand rejected under 35 U.S.C. §102(b) over Anbazhagan et al. (Cancer Research, 1999. Vol 59, 5119 - 5122). Applicants respectfully traverse the rejection.

The present claims were set forth above.

The Examiner argues that the Anzbazhagan reference discloses a gene chip array containing 18210 cDNA clones obtained from Gene Discovery Array Human I used to determine differentially expressed genes in SLSC, normal bronchial epithelial cells, pulmonary carcinoids and infiltrating astrocytic brain cancers...and (the) array comprises genes that are differentially expressed in SCLC, TC, AC and normal tissue." Applicants disagree.

The Anbazhagan reference examines broad profiles of gene expression to determine similarities and differences between tumors. (see, e.g. abstract p.5119). Anbazhagan admits that "although a study of gene expression of SCLC using cDNA arrays was initiated with a goal to identify specific gene expression changes related to the pathogenesis of SCLC" the study became directed to determining "how similar these tumors are to one another by comparing the gene expression profiles of the different tumor samples." (p.5119). The Table on page 5121 of the Anbazhagan reference shows the expression levels of selected genes with differential levels of expression among five samples examples. None of the genes identified correspond to GGH as presently claimed.

Accordingly, the Anbazhagan reference does not teach or suggest all the limitations of the instant claims. Applicants respectfully request that the rejection be withdrawn.

Claims 20 – 27 stand rejected under 35 U.S.C. §102(a) over Virtanen et al. (PNAS, 2002. Vol. 99, 12357 - 12362). Applicants respectfully traverse the rejection.

The present claims were set forth above.

The Examiner argues that the Virtanen et al. reference discloses a microarray that comprises 6,671 unique genes which was used to determine differential gene expression profile in SCLC, LCNEC, TC, AC and normal tissue...(and) therefore disclose the claimed microarray." (Office Action, p.7).

The Virtanen et al. reference reports microarray-based expression profiling of lung tumors and cell lines. The microarray used incorporated an estimated 6,671 unique genes. Virtanen et al. teach identification of genes differentially regulated between tumors and cell lines (see, e.g. Figure 2). None of the genes identified correspond to GGH as presently claimed.

Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claims 20 – 28 stand rejected under 35 U.S.C. §102(b) over Cherkaoui-Malki et al. (Gene Expression, 2001. Vol. 9, 291 - 304). Applicants respectfully traverse the rejection.

The present claims were set forth above.

The Examiner argues that "Cherkaoui-Malki et al. disclose a microarray chip obtained from Incyte genomics, which comprises 6973 genes, and wherein one of the genes is CPE. Although this chip is not used to identify genes differentially expressed in neuroendocrine tumor, it meets the limitation of a microarray comprise genes distinguishably arrayed in spaced apart regions and comprises more than 10 genes, wherein at least one of the gene is CPE as recited in claim 28."

Applicants disagree. The Cherkaoui-Malki reference identifies peroxisome proliferator-activated receptor alpha target genes in mouse liver. Accordingly, the work described by Cherkaoui-Malki is based on the analysis of mouse liver, for which they would have used a mouse cDNA microarray. Applicants direct the Examiner's attention to page 293 of the Cherkaoui-Malki reference, where this work is described:

> Poly(A)+ RNA was labeled with Cy3 and Cy5 fluorescent dyes for microarray hybridization on UniGene **mouse cDNA microarray** (Incyte Genomics, St.Louis, MO), as described elsewhere (77). cDNA mouse clones, corresponding to spotted cDNAs on the microarray, were obtained from Incyte Genomics, amplified and sequenced to verify the correct identity of each clone. (emphasis added)

Unlike the Cherkaoui-Malki reference, the present inventors use a **human** cDNA library. Accordingly, the genes are different and not taught by the Cherkaoui-Malki reference.

Applicants respectfully request that the rejection be withdrawn.

For the reasons provided, Applicant submits that all claims are allowable as written and respectfully requests early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

A two month extension of time is requested. It is believed no additional fees are due, however should any fee be due, the Commissioner is authorized to charge such fee to our Deposit Account, No. 04-1105, Reference 63139(47992). Any overpayment should be credited to said Deposit Account.

Respectfully submitted,

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